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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,315	09/08/2003	Mark James O'Connor	MEWE-016	2162

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,315	O'CONNOR ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *3,6,8 and 12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/30/03+08/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Reassignment Affecting Application Location

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648, Emily Le.

Miscellaneous Communication

2. To clarify the record, the following item(s) should not have been included in the restriction requirement issued to Applicant:

a) the template or draft of a 103 rejection, and

b) the rejoinder between product and method statement.

Election/Restrictions

3. Applicant's election with traverse of Group II in the reply filed on 07/13/2005 is acknowledged. The traversal is on the ground(s):

a. The Office has improperly separated out the features of claim 1 as if they were entirely different inventions. Claim 1 is a proper generic claim, and any restriction would most require an election of species in the group, not a restriction to separate inventions.

The above summarized submission has been considered, however, it is not found persuasive. In the instant, the Office has the discretion to issue either restriction between or among inventions or species.

Additionally, it is recognized that the restriction requirement failed to recognize claim 1 as a linking claim, the claim that links inventions I-IV. A restriction requirement

among the linked inventions is subject to the nonallowance of the linking claim(s), claim I. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

b. An invention that is directed to in vitro practice is not distinct from an ex vivo practice.

Applicant's submission has been considered, however, it is not found persuasive. MPEP § 806.04 and MPEP § 808.01 sets forth that inventions are distinct if it can be shown that the inventions are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects. In the instant, the two practices are patentably distinct from one another because the inventions have different modes of operation. An ex vivo practice requires the extraction of cells from a host for treatment then subsequently returned to the host. An in vitro practice does not require the subsequent return of the cells to the host.

c. The Office has improperly separated Groups I and III, and Groups II and IV. A search of Group II should fully encompass Group IV, as exemplified by the identical classification the Office has assigned to the groups. The same analysis applies to Group I should fully encompass Group III.

Applicant's submission has been considered, however, it is not found persuasive. The fact that the inventions share the same class and subclass does not mean that a search for one invention would fully encompass a search for another invention. The Office uses the classification system to establish a relation between an invention and the art, art status. In the instant, the Office finds that the inventions relate the same art. However, this finding does not equate to a same search. The field of search for Group I would be inhibition of RAD-52 protein production, and the field of search for Group III would be inhibition of RAD-52 and DNA binding activity. These fields of search differ from one another. Furthermore, MPEP § 806.04 and MPEP § 808.01 sets forth that inventions are distinct if it can be shown that the inventions are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects. In the instant, the invention of Group I is patentably distinct from the invention of Group III because each has a different mode of operation than the other. The invention of Group I is directed to the promotion of retroviral integration by inhibiting the production of RAD-52 protein; whereas, invention of Group III is directed to the promotion of retroviral integration by inhibiting the binding of DNA by RAD-52. The same analysis applies for the invention of Group II and the invention of Group IV.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

4. Claims 1-20 are pending. Claims 3, 6, 8 and 12-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 07/13/2005. Claims 1-2, 4-5, 7 and 9-11 are under examination.

Specification

5. The disclosure is objected to because of the following informalities: The claims are not the object of a sentence starting with "I (or we) claim," "The invention claimed is" (or the equivalent). Instead, the claims are the object of a sentence starting with "claims". This is not the equivalent of "I (or we) claim," "The invention claimed is" or the likes. MPEP 608.01(m) [R-3] requires that each claim be the object of a sentence starting with "I (or we) claim," "The invention claimed is" (or the equivalent). Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-2, 4-5, 7 and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2, 7 and 9-11 are indefinite because the claims are incomplete for the omission of essential elements, wherein such omission amounting to a gap between the elements. See MPEP § 2172.01. In the instant, the claims specify that the claimed invention is a process, a process for promoting the integration of retroviral vectors into mammalian cells. Additionally, the claims specify that the promotion of retroviral vector integration into mammalian cells can be achieved by inhibiting RAD52 DNA-binding activity in the cell. However, the claims do not specify a procedure or active method steps to conduct in order to inhibit RAD52 DNA-binding activity to promote the integration of retroviral vectors into cells. Without a procedure or active method steps to conduct, it is unclear how the inhibition of RAD52 DNA-binding activity can be accomplished.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2, 4-5, 7 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a method of promoting the integration of a retroviral vector into a mammalian cell comprising inhibiting RAD52 DNA binding activity into the

cell. In the instant, with the exception of claims 4-5, none of the claims specify a procedure to accomplish the inhibition RAD52 DNA binding activity. Claims 4-5 specify that the procedure to conduct is to contact the mammalian cell with a double stranded RNAi or an antisense RNA.

The focus of this rejection is directed at the lack of adequate written description for compositions, including the double stranded RNAi or an antisense RNA, that inhibit RAD52 DNA binding activity. The claims, with the exception of claims 4-5, are not specific to a composition for use with the claimed method; whereas, claims 4-5 are not limited to a particular double stranded RNAi and an antisense RNA. Thus, the claims are directed to a genus of compositions that inhibit RAD52 DNA binding activity, including a genus of double stranded RNAi and an antisense RNA.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient description of a representative number of species by i) actual reduction to practice, ii) reduction to drawings, or iii) disclosure of relevant identifying characteristics. Examples of factors to be considered for the latter requirement include:

- disclosure of complete or partial structure,
- physical and/or chemical properties,
- functional characteristics,
- correlation between structure and function, and
- methods of making.

Each of the listed criteria is addressed in turn below.

i) sufficient description of a representative number of species by actual reduction to practice: The specification teaches SEQ ID NO: 1, a single 21 nucleotide duplex small interfering RNA, that interferes with RAD52 expression. Specifically, the specification teaches that the presence of SEQ ID NO: 1 in cells reduces RAD52 expression in the cells. The specification does not teach any other sequences capable of interfering with RAD52 expression. In the instant, the specification only teaches one sequence.

Additionally, it is noted that the specification does provide generic teachings of compositions that inhibit RAD52 DNA binding activity. The specification notes that RAD52 may be modulated by targeting a product of another gene, e.g., a protein that affects RAD52 expression, stability or activity. However, that is all that the specification provided. The specification does not teach what types of gene products can be use as a target to modulate RAD52 expression, stability and activity.

ii) sufficient description of a representative number of species by reduction to drawings: The drawings do not contain a description of any compositions, including any double stranded RNAi and an antisense RNA, for inhibiting RAD52 DNA binding activity.

iii) sufficient description of a representative number of species by disclosure of relevant identifying characteristics:

- disclosure of complete or partial structure: The disclosure only provides for one double stranded RNAi sequence, SEQ ID NO: 1, for use with the claimed invention. No other double stranded RNAi or a single antisense

RNA sequence is provided in the specification. Nor any other compositions are disclosed.

Additionally, as discussed above, the specification does provide generic teachings of compositions that inhibit RAD52 DNA binding activity. The specification notes that RAD52 may be modulated by targeting a product of another gene, e.g., a protein that affects RAD52 expression, stability or activity. However, that is all that the specification provided. The specification does not teach what types of gene products modulate RAD52 expression, stability and activity.

- physical and/or chemical properties: The disclosure does not provide any guidance pertaining to the specific or particular physical or chemical properties that the double stranded RNAi and an antisense RNA must have in order to inhibit RAD52 DNA binding activity. Nor does the specification provides any guidance pertaining to the specific or particular physical or chemical properties the gene products must also possess.
- functional characteristics: From the specification and the claims, it is presumed that the composition for use with the claimed composition must be able to act as an inhibitor of RAD52 DNA binding activity.
- correlation between structure and function: While the functional characteristic of compositions that inhibit RAD52 DNA binding activity is readily apparent from the specification and the claims, no correlation

between the required functional characteristic and a structure that is responsible for the required functional characteristic can be ascertained from the specification or the claims.

- Methods of making the product: Generic methods of making gene products, e.g., proteins, double stranded RNAi and antisense RNA are well established in the art. However, methods of making gene products, double stranded RNAi and antisense RNA that inhibit RAD52 DNA binding activity is not well established in the art. In the absence of a correlation between structure and function, disclosure of complete structure for each species, detailed physical and/or chemical properties for gene products, double stranded RNAi and antisense RNA that are specific for the required functional characteristic, those skilled in the art would not know how to make the gene products, double stranded RNAi and antisense RNA required for practice with the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the disclosure only provides one species of double stranded RNAi that interferes with the binding of RAD52 with DNA. The disclosure does not teach of any

other species. No other double stranded RNAi or a single antisense RNA sequence is provided in the specification. Additionally, not a single gene product that modulates RAD52 is disclosed. Nor does the disclosure provide any guidance concerning the required functional characteristic, inhibition RAD52 DNA binding activity, and the structure that is responsible for the required functional characteristic. In the instant, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus compositions based on the teaching from the specification. And therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, double stranded RNAi having the sequence of SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-2 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al.[1] in view of Van Dyck et al.[2]

The claims are directed to a method of promoting integration of a retroviral vector into the genome of a mammalian cell comprising inhibiting RAD52 DNA-binding activity in the cell.

Li et al. teaches the integration of a retroviral vector into a mammalian cell.

Li et al. does not teach the inhibition of RAD52 DNA-binding activity binding to promote retroviral integration in cells.

However, Li et al. does note that the binding of the Ku protein to DNA promotes the establishment of retroviral integration into cells. [Abstract] Van Dyck et al. teaches that the RAD52 protein competes with the Ku protein for DNA. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to inhibit the production of RAD52 protein in a cell. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to enhance integration of retroviral vectors into cells. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the absence of RAD52 makes more DNA available for binding with the Ku protein.

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[1] Li et al. Role of the non-homologous DNA end joining pathway in the early steps of retroviral infection. The EMBO Journal, 2001, Vol. 20, No. 12, 3272-3281.
[2] Van Dyck et al. Binding of double-strand breaks in DNA by human Rad52 protein. Letters to Nature. 1999, Vol. 398, 728-731.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

14. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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E.Le